

EXTENDED REPORT

Colour vision testing as an aid to diagnosis and management of age related maculopathy

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Aim: To provide a simple test that detects the onset of age related maculopathy (ARM), and can be used to monitor its severity.

Methods: Colour contrast sensitivity was measured using computer graphics techniques. Colour thresholds were measured along tritan and protan colour confusion axes in the presence of dynamic luminance noise. Thresholds were determined separately for two sizes of optotypes (6.5° and 1.5°). Natural pupils were used. Normal values for the test have been established.

Results: In all patients with unilateral age related macular degeneration, the smaller optotype was invisible in that eye and in almost all, the larger optotype could not be seen. In the symptomless fellow eyes (with ARM) the larger optotype thresholds were raised. The degree of loss was larger for tritan. For the smaller optotype, protan thresholds were elevated in the majority of patients. Tritan losses were greater and disproportionate to the loss seen with the larger optotype. Every person including those with minimal fundal changes had tritan test results for 1.5 degree optotypes >2 SD above the normal mean. Tritan thresholds varied with the severity of the ARM.

Conclusions: The test is sensitive, simple and quick to administer, and easy for patients. Therefore, it should be useful in detecting and monitoring elderly people with age related changes in their fundi before irreversible loss of vision has occurred.

It is common for ophthalmologists to see patients with age related maculopathy (ARM) only after considerable unilateral irreversible visual loss has occurred.^{1–5} A screening programme involving simpler tests that could be carried out by non-specialists^{6–10} is needed to identify “at risk” patients who have no symptoms. Even if methods of treatment are not very efficacious, the condition is so common that screening would result in very considerable sight saving.^{9–11–12} Various methods have been proposed. The results from electro-oculograms (EOGs), non-photoc EOGs, electroretinograms (ERGs), pattern electroretinograms (PERGs), and multifocal ERGs are controversial.^{13–23} Psychophysically determined losses of rod sensitivity have been reported to occur before other symptoms.^{24–26} Slight losses of visual acuity occur in patients with large soft drusen, and there may be slight and various changes with Amsler chart.²⁷ Various losses of cone function have been investigated.^{18–28–29} Colour vision testing with the D-15 or 100 hue test has not been found useful.^{27–29} However, it has been reported that blue on yellow perimetry (short wavelength automated perimetry, SWAP)³⁰ or colour matching³¹ can detect early changes in ARM. Colour contrast sensitivity testing^{32–40} offers significant advantages in speed and ease of administration, important for screening purposes,^{36–7–39–41–42} and although not widely employed in ARM,^{41–44} small losses occur in otherwise symptomless patients after a period as short as a year.⁴¹ This paper is the first report on the possibility of screening using (in a small series) a modified method of colour contrast sensitivity testing. Apart from technical modifications to software and hardware, we investigated the effect of using a flashed smaller optotype confined to the central macula. The sensitivity for detecting ARM was thereby improved and the results suggest how screening for ARM might be carried out in larger surveys.

METHODS

Equipment

Colour contrast sensitivity was measured with a revised version of the equipment used in previous work.^{32–34} In this test, isoluminant coloured optotypes are generated on a calibrated monitor, on a white background of ~20 cd.m² and the colour difference between the optotypes and a neutral (white) background is altered until the threshold of visibility is obtained. The most important software improvements for the new model were (1) the superimposition of random dynamic luminance noise on the coloured optotype that the patient had to name.⁴⁵ Such noise effectively masks any luminance clues in recognising the optotype (colour contrast sensitivity is unaffected by such luminance masking.⁴⁰ The luminance noise contrast defined as $(L_{\max} - L_{\min}) / (L_{\max} + L_{\min})$ was 0.4, greater than any luminance difference between the optotype and the surround. (2) In addition, the psychophysical routines were made more efficient so the test stops automatically when a preset degree of precision has been attained. Between six and 15 observations, at 3–5 second intervals are required to establish a threshold. The protan and tritan colour confusion lines along which the colours were modulated formed the major and minor axes of a MacAdam ellipse centred on white.⁴⁵ We used two differing sizes of optotype, subtending 6.5 and 1.5 degrees, viewed at 1 metre.

Calibrations

The results of the test are expressed as a percentage of the maximum modulation of colour possible along the chosen colour confusion line.

Abbreviations: AMD, age related macular degeneration; ARM, age related maculopathy; EOG, electro-oculogram; ERG, electroretinogram; PERG, pattern electroretinogram

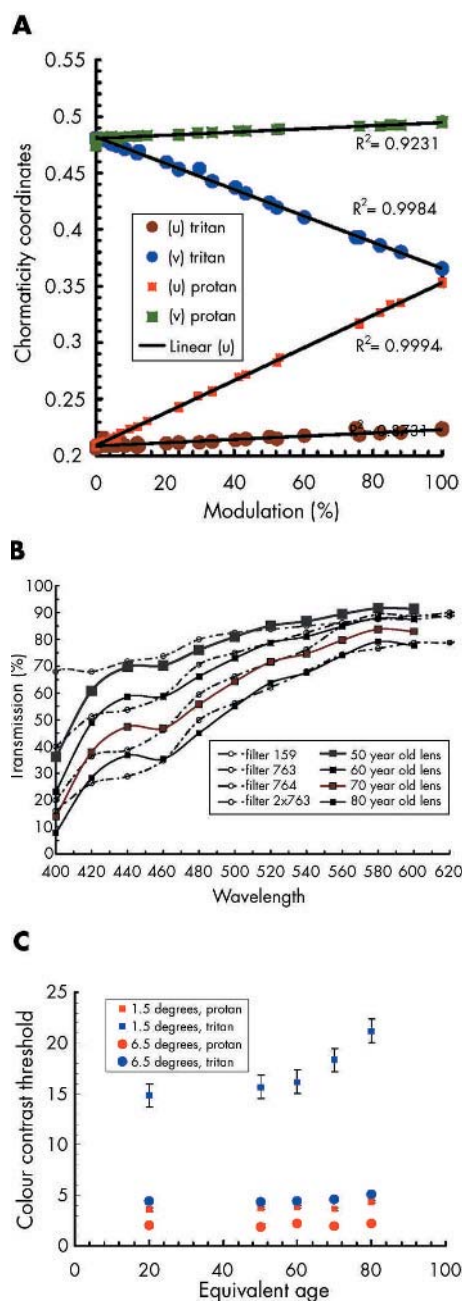


Figure 1 (A) Changes to measured chromaticity with change of modulation depth. (B) Reduction in lens transmission as a function of age⁴⁶ compared to the transmission of filters for ages 50, 60, 70, and 80. The filters were as follows; plastic filters provided by Lee Filters, Ltd, UK. For 50 year old data No 159, for 60 year old No 763, for 70 year old No 764, for 80 year old two layers of No 763. (C) Changes in thresholds with yellow filters in 20 year old subjects. The vertical bars are plus or minus 1 SD, and are within the symbols except for the smaller tritan optotypes.

Figure 1A shows the relation between measured chromaticity and displayed modulation, and the correlation coefficients for the four sets of measurements (all >0.99). The standard errors of the slopes are between 0.00001 and 0.000055 chromaticity units. A 1% change in threshold is equal to a displacement in colour space of 0.0012 unit. The change in luminance of the optotypes from 0 to 100%

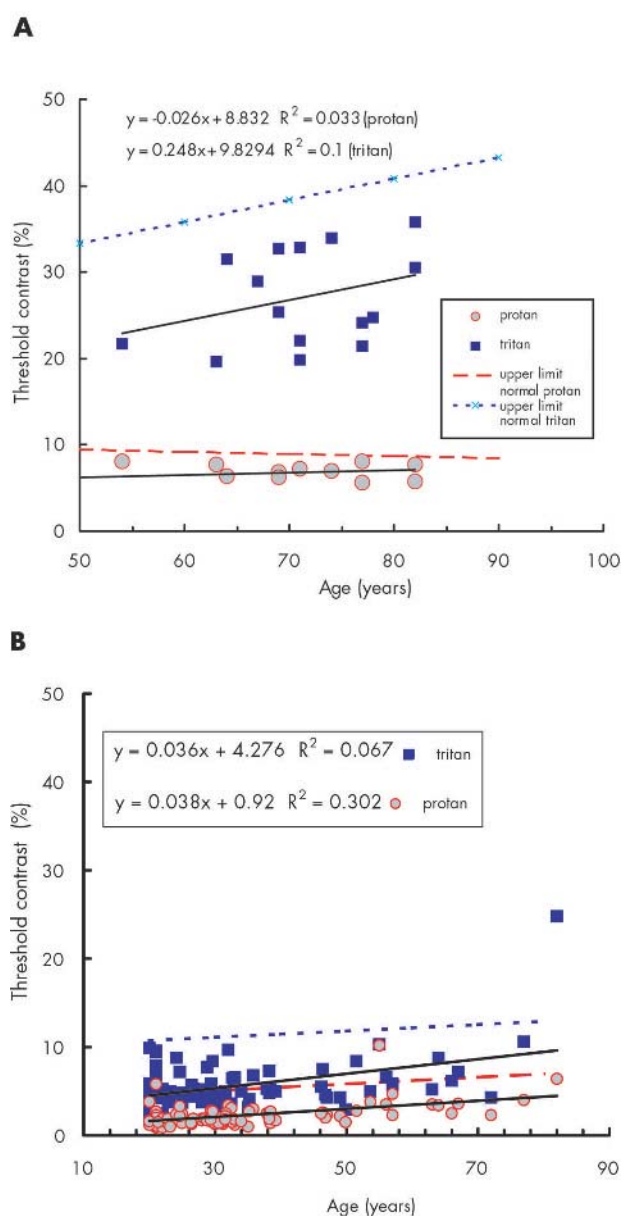


Figure 2 (A) Normal results for smaller optotypes in an older population. The trend line equations are shown. The blue broken line is 2 SDs above the normal mean values for tritan thresholds, and the red broken line is the upper limit of normal for the protan threshold. (B) Normal results for larger optotypes in an older population. The trend line equations are shown and refer to values obtained in patients with measurable thresholds (<100%). The blue broken line is 2 SDs above the normal mean values for tritan thresholds, and the red broken line is the upper limit of normal for the protan threshold.

modulation was measured as 0.8 cd.m² for protan letters and 0 for tritan letters. Variations in the optical density of macular pigmentation, or changes due to lens yellowing that occur with age might also affect thresholds. In eight 20 year old subjects, with 3 mm artificial pupils, thresholds were determined using a variety of yellow filters that approximated to the changes in lens transmission.⁴⁶ Figures 1B and C show the filters and the changes in threshold associated with their use. Only with the smaller tritan letters and filters associated with 70 and 80 year old people do thresholds increase slightly, consistent with recent work.⁴⁷

Normal values

1.5 Degree optotypes

Sixteen elderly people were recruited, spouses of members of the Macula Disease Society, the authors, their friends, and relations. Three of the people initially recruited as normals proved on examination to have early fundal changes of ARM, abnormal colour vision, and (in two cases) abnormal alcohol responses in the EOG.^{48,49} They were excluded. All the rest had no systemic or eye disease that might affect vision, normal fundi, and normal corrected visual acuity. The mean age was 71.75 (range 57–82). The mean visual acuity was 0.93 (range 0.7–1.5). Contrast thresholds were protan: 6.63% (SD 1.22%) and tritan: 26.8% (5.5%); seven were female and nine male. Female thresholds were 6.9 (protan) and 28.0 (tritan). Male thresholds were 6.4% (protan) and 26.0% (tritan). The 65–74 year old thresholds also differed insignificantly from the 75–84 year old group. For protan, the means were 7.0% and 6.4% respectively. For tritan the values were 28.0% and 27.7% respectively. These tritan values are very similar to those of young people, tested with yellow filters (fig 1C).

Figure 2A shows the results for 1.5 degree optotypes. The regression of threshold on age is insignificant ($r^2 = 0.068$). The slope of the relation between age and threshold is 0.864, with a standard error (SE) of 0.71, and for protan 0.264, with an SE of 0.167—that is, not significantly different from zero. The broken lines in the figure represent upper limits of normal, obtained by fitting a least squares linear regression to the data, finding the mean value at each age and adding twice the value of the standard deviation of the entire group. Should there be a regression with age, the actual SD at any age would be smaller than assumed. Alternatively an upper limit of $(26.8 + (2 \times 5.5)) = 37.8$ could be used, but this is a less severe criterion for anyone aged more than 73.

6.5 Degree optotypes

These have been used in the investigation of other conditions, and 96 normals, mean age 34.6 (range 20–81) were available (fig 2B). The mean protan threshold is 2.4 %, (SD 1.5) and the mean tritan, 5.7% (2.9). Forty per cent were female. The mean age of male and female groups was the same, as were the colour thresholds and their regression on age. Disregarding the one tritan outlier in figure 2B, regression analysis shows a slope of 0.04 threshold units per year, with an SE of 0.01 for both tritan and protan. Thus, there is a small though significant change with age that is the same for both protan and tritan letters, in agreement with data of Nguyen-Tri *et al.*⁴⁷ For consistency, the upper limits of normal have been defined as for figure 2A. Allowing for the very small effect of age on mean threshold, large protan optotype thresholds are smaller than those of 1.5 degree optotypes by a factor of 1.9. For tritan, the ratio is 3.2, reflecting the relative paucity of blue cones in the central 1.5 degrees.

People with ARM

Three people who volunteered as elderly normals and were found to have minimal fundal signs of ARM are included in this group. Twenty one other patients with various stages of ARM were recruited from meetings of the Macular Disease Society. The entry criteria were general good health, mobility unimpaired; no systemic hypertension; no diabetes; no other systemic disease; no other ocular disease (except minimal lenticular opacity); one eye may have loss of vision due to AMD; fellow eye must have no symptoms and visual acuity ≥ 0.6 . The mean age was 76. A subset of these patients had been subject of other investigations.⁴⁹ Four of the patients were not tested with 6.5 degree optotypes. All had been investigated in UK eye departments and had been given firm diagnoses of ARM. All were clinically re-examined and a

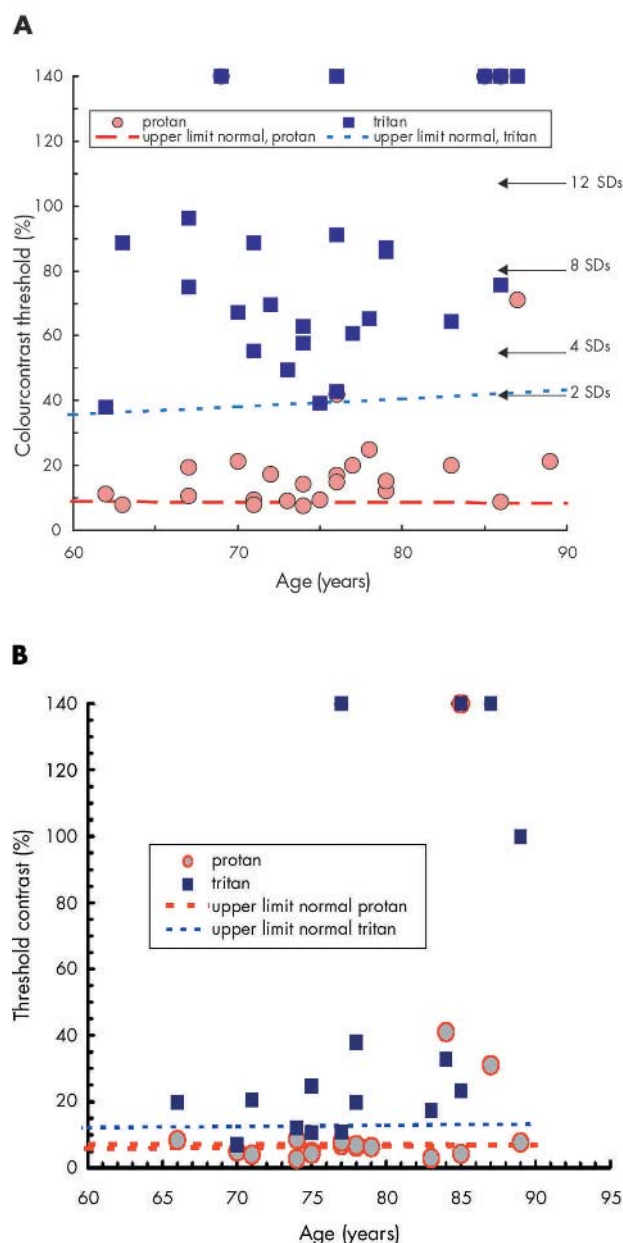


Figure 3 (A) Thresholds for 1.5 degree letters in patients with ARM. The upper limits of normal are transferred from figure 2. Note the difference in vertical scaling. (B) Thresholds for 6.5 degree letters in patients with ARM. The upper limit of normal is transferred from figure 2. Note the difference in vertical scale between this figure and figure 2.

history taken. The three least affected had good vision in either eye. Copies of clinical records were obtained. In some cases, fluorescein angiographic results were available. In a subgroup of 16, reported by us previously,⁴⁹ fundi were photographed. Because of difficulties in some patients with full dilatation of the pupils, and media that were not completely transparent, 25° stereoscopic views did not give adequate results in all cases. To maintain consistency, we compromised and took 45° views, enlarging them to $\times 40$, and used the grid and definitions and scoring procedures laid out by Bird *et al.*⁵⁰ to grade and rank the severity of the changes within the group studied.⁴⁹ All patients gave informed consent conforming to the second declaration of Helsinki.

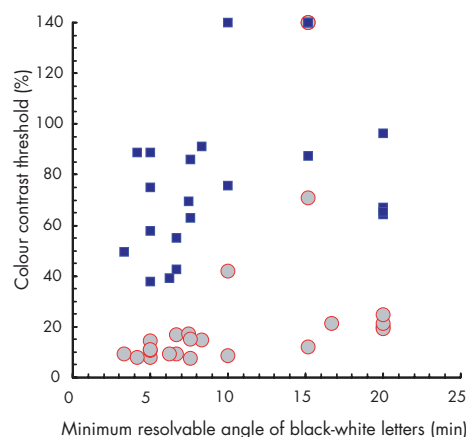


Figure 4 Relation of thresholds to visual acuity. 5' arc indicates an acuity of 1.0, and 50', and acuity of 0.1 (this method of plotting is designed to present the result more clearly).

RESULTS

Colour contrast thresholds in patients' worse eyes

Most of the patients had a considerable degree of loss of visual acuity in one eye. In all such eyes the smaller coloured letters could not be identified at all. The large tritan optotypes were read by only three individuals at 100% contrast, while four could distinguish protan coloured letters at 100% contrast. Therefore, the analysis below is confined to the better, fellow eyes.

Better eyes, 1.5 degree optotypes

Figure 3A shows the results for the smaller optotypes. If the optotypes could not be read at all, thresholds are arbitrarily given the value of 140%.

Both the 1.5 degree protan and tritan thresholds increase with age. The slope for protan is 0.26 threshold units/year, with an SE of 0.167, $r^2 = 0.12$ while for tritan the values are 0.86, and 0.71, $r^2 = 0.08$. These results are not significant, but no such increase with age was seen in the normal group. The tritan losses are greater than the protan. Thus, 11 of the protan results are abnormal and in three patients the letters could not be identified at all. The 17 tritan thresholds are very high, much above the upper limit of normal and in five the threshold could not be measured. Thirteen of the protan but only seven of the tritan thresholds are less than twice the normal values. The probability of this being the result of chance (χ^2) is 0.014. Figure 4 shows the relation of thresholds of 1.5 degree optotypes as a function of the reciprocal of visual acuity. For visual acuity of <0.7 , there is no obvious relation between colour contrast threshold and acuity.

Better eyes, 6.5 degree optotypes

Even though the protan results are frequently near normal with large optotypes (fig 3B), the tritan thresholds are clearly elevated. Three "better eyes" could not see any 6.5 degree tritan letters and only one could not see any 6.5 degree protan letters. Two other protan results are considerably higher than the upper limit of normal. The remainder of the

protan results cluster about the upper limit of normal. Nine of the tritan thresholds are considerably higher than the upper limit of normal, and only three are below it. Ten of the protan results and four of the tritan are less than twice the normal values. The probability of this being due to chance (χ^2) is 0.002.

Interactions

For large letters, the protan and tritan thresholds are well correlated ($r = 0.64$) but for small, the correlation is much less ($r = 0.21$). The correlation between large and small letters for protan is 0.87, while for tritan the correlation is poorer $r = 0.55$. These results exclude those in whom the optotypes could not be seen. These correlations reflect the selective increase in threshold seen with the smaller tritan optotypes.

Relation to fundus appearance

In a subgroup of patients fundal appearances were ranked,^{49 50} and compared to the colour contrast results, using Spearman's rank order correlation methods. The correlation coefficients are given in table 1. For $n = 14$, the minimum level for a 95 % rejection of the null hypothesis is 0.545, so only the result with the smaller tritan letters is not significant. This is probably because of the large number of results which are "tied"—that is, have equal rank because no letters could be seen. Again, this reflects the selective increase in threshold with the smaller tritan optotypes. The highest value of the coefficient is given from the results on large tritan letters.

Figure 5 summarises the change in threshold with clinical state. On the left is a nearly normal fundus, with one or two large soft drusen. The larger optotype thresholds are within normal limits. The small optotype tritan threshold is high, but just less than 2 SDs above the mean. The central image shows a fundus with many confluent drusen. The patient's vision was excellent and there were no symptoms. The central retinal region shows up as darker, because of areas of retinal and retinal pigment epithelium thinning showing choroidal coloration. Protan thresholds are normal, but even the larger tritan optotype gives an abnormal result. On the right is the fundus image of a patient who has, additionally, oedema and pigmentation. Visual acuity is reduced, and all colour contrast tests give very abnormal results.

DISCUSSION

There is an enormous loss of the ability to recognise tritan optotypes in early ARM, unrelated to the yellowing of the lens or to visual acuity but related to the severity of the retinal changes and to age. The distinction from normals is much greater than that found by older methods of assessing colour vision.^{30 31} Previous reports on colour contrast sensitivity in ARM^{41–44 51} are consistent with our work which also investigates the findings in patients at various stages. The reason that the present technique appears more successful may be that the optotypes were flashed briefly. Eye movements could not assist the recognition of the letters, so while a coloured region on the screen could be seen, the letter could not be identified. It is possible that there are small perifoveal scotomas for blue in these patients that impede letter discrimination. Whatever the reason, there is an almost

Table 1 Correlations between colour test and fundus appearances

Image	6.5° protan	6.5° tritan	1.5° protan	1.5° tritan
Spearman correlation* (n = 14)	0.664	0.714	0.711	0.470

*Fundus appearance correlated to colour vision threshold.



Figure 5 See text.

JW 63 years VA = 1.0		AW 71 years VA = 1.0		DB 69 years VA = 0.3	
Thresholds for Large Letters (6.5°)					
protan	tritan	protan	tritan	protan	tritan
5.3 %	9.1 %	5.7 %	19.9 %	65.6 %	not seen
Thresholds for small Letters (1.5°)					
protan	tritan	protan	tritan	protan	tritan
7.9 %	32.7 %	7.9 %	88.1 %	not seen	not seen

Suspicious results circled; abnormal results, underlined

complete separation between the patient and normal results, even in the milder cases.

Age as a confounding factor in measurements of loss of colour contrast

In older subjects the lens scatters more and loses transparency especially at shorter wavelengths. This leads to a small increase in luminance and contrast thresholds—0.15 log unit per decade,⁵² or 0.19 log unit/decade,⁵³ or 0.7 dB per decade.⁵⁴ The relation between age and threshold has been reported as linear,⁴⁷ as found in this paper. Pupillary diameter also decreases with age, and the reduction in luminance can change colour contrast thresholds. None of these changes is significant in relation to the very large changes in colour contrast sensitivity found in our subjects with ARM. In the patients, threshold may increase more rapidly with age than in the normals. The cause of this difference may simply be that the severity of ARM progresses with time.

Colour contrast as a screening test for ARM

An optotype test is familiar and quick. Untrained people can administer it. These qualities are important for screening. With smaller letters, many of our patients had thresholds higher than could be measured. Even with mild fundal changes in people newly diagnosed and previously thought to be normal, tritan thresholds may be significantly elevated. Tritan colour contrast thresholds increase greatly before the patient becomes in immediate danger of developing geographic atrophy or disciform degeneration. There is a correlation between threshold and degree of abnormality in the fundus. These results are novel and suggest it would be possible to use the system for monitoring the onset and progress of ARM. In some of the cases, repeat testing after 9 months has shown deterioration (paper in preparation), and such a deterioration with time has been reported previously.⁴¹ The usefulness of the test in practice would be to distinguish between a very large number of elderly people who have mild retinal changes, and the few with much higher and increasing thresholds who need treatment or detailed ophthalmological investigations. Criteria could be set that would distinguish such a subgroup. For example,

referral from a primary screening clinic might occur when the person was unable to distinguish small tritan letters at 100% modulation, or large tritan letters at 30% modulation (6 SD above the normal mean, see fig 3). The colour contrast test thus has potential for an improvement in patient management. Our results suggest that the referral criterion could be adjusted to suit local needs and the availability of adequate treatment and would reduce the personal and institutional costs of loss of vision. In common with all such tests it is not possible to ensure that the test will only pick up a specific pathology, but other acquired colour vision deficiencies require ophthalmological investigation.

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